10/653,677

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JUL 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 4	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 5	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 6	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 7	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 8	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 9	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 10	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 11	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 12	SEP 27	STANDARDS will no longer be available on STN
NEWS 13	SEP 27	SWETSCAN will no longer be available on STN
NEWS 14	OCT 28	KOREAPAT now available on STN

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:27:00 ON 05 NOV 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:27:06 ON 05 NOV 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 NOV 2004 HIGHEST RN 774506-08-0
DICTIONARY FILE UPDATES: 3 NOV 2004 HIGHEST RN 774506-08-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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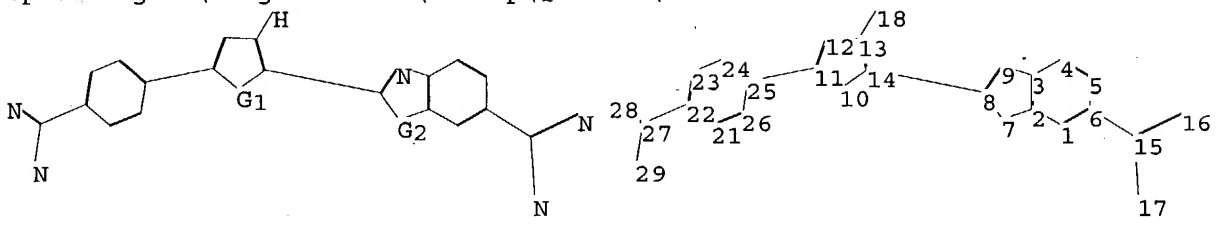
Uploading C:\Program Files\Stnexp\Queries\10653677.str



chain nodes :
15 16 17 18 27 28 29
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 21 22 23 24 25 26
chain bonds :
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ring bonds :
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21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
2-7 3-9 6-15 7-8 8-9 8-14 10-11 10-14 11-12 11-25 12-13 13-14 13-18
15-16 15-17 22-27 27-28 27-29
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 21-22 21-26 22-23 23-24 24-25 25-26
isolated ring systems :
containing 1 : 10 : 21 :

G1:O,S

G2:O,N

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Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:CLASS  16:CLASS  17:CLASS  18:CLASS  21:Atom
 22:Atom  23:Atom  24:Atom  25:Atom  26:Atom  27:CLASS  28:CLASS  29:CLASS



L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 14:27:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 14:27:30 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      9 TO ITERATE

100.0% PROCESSED       9 ITERATIONS                                  9 ANSWERS
SEARCH TIME: 00.00.01

L3            9 SEA SSS FUL L1

=>  d scan

L3   9 ANSWERS   REGISTRY  COPYRIGHT 2004 ACS on STN
IN   1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-
     furanyl]-, dihydrochloride (9CI)
MF   C19 H16 N6 O . 2 Cl H
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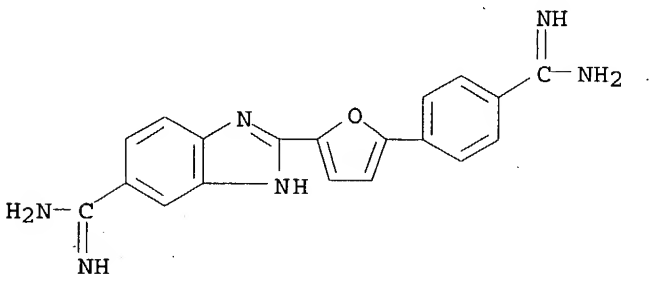

●2 HCl

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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
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=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       155.84     156.05

FILE 'CAPLUS' ENTERED AT 14:28:04 ON 05 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 5 Nov 2004  VOL 141 ISS 20
FILE LAST UPDATED: 4 Nov 2004  (20041104/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4          20 L3

=> d l4 ibib hitstr abs 1-20

L4   ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:791709  CAPLUS
DOCUMENT NUMBER:         141:325174
TITLE:                   Dicationic biphenyl benzimidazole derivatives as
                         antiprotozoal agents
AUTHOR(S):               Ismail, Mohamed A.; Brun, Reto; Wenzler, Tanja;
                         Tanious, Farial A.; Wilson, W. David; Boykin, David W.
CORPORATE SOURCE:        Department of Chemistry and Center for Biotechnology
                         and Drug Design, Georgia State University, Atlanta,
                         GA, 30303-3083, USA
SOURCE:                  Bioorganic & Medicinal Chemistry (2004), 12(20),
                         5405-5413
                         CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER:               Elsevier Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
IT   216308-19-9
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (dicationic biphenyl benzimidazole derivs. as antiprotozoal agents)
RN   216308-19-9  CAPLUS
CN   1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-
     furanyl]- (9CI)  (CA INDEX NAME)
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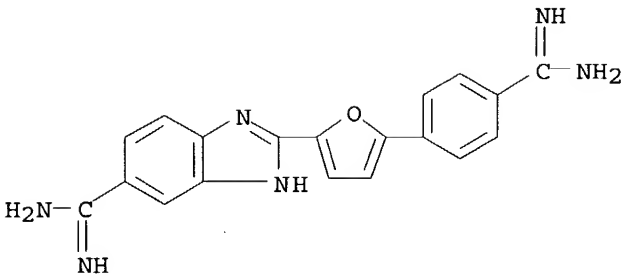


AB A series of biphenyl benzimidazoles diamidines were synthesized from their resp. diamidoximes, through the bis-O-acetoxyamidoxime followed by hydrogenation in glacial acetic acid/ethanol in the presence of Pd-C. The target compds. contain hydroxy and/or methoxy substituted 1,3-Ph groups as the central spacer between the two amidino bearing aryl groups. All of the diamidines showed strong DNA affinities as judged by high ΔTm values with poly(dA·dT)2, which varied with structure and is discussed. Seven of the nine new diamidines gave in vitro IC50 values of approx. 30 nM or less vs. Trypanosoma brucei rhodesiense (T.b.r.). Generally the diamidines were less active vs. Plasmodium falciparum (P.f.), however one compound exhibited excellent activity with an IC50 value of 2.1 nM. Five of the nine diamidines exhibited excellent in vivo activity in the trypanosomal STIB900 mouse model giving 3/4 or 4/4 cures at dosage of 20 mg/kg i.p. and three showed similar efficacy at dosage of 10 mg/kg or lower.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:991295 CAPLUS
DOCUMENT NUMBER: 140:35966
TITLE: Amidine derivatives for treating amyloidosis and neurodegenerative diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo; Tidwell, Richard R.; Boykin, David
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA; Georgia State University Research Foundation, Inc.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103598	A2	20031218	WO 2003-US17992	20030609

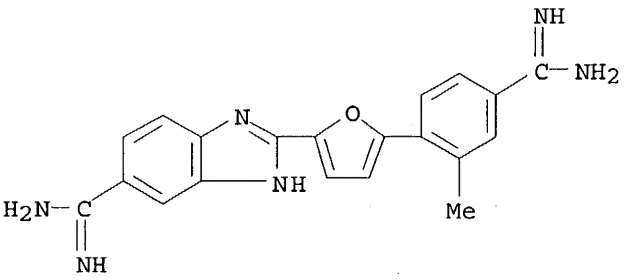
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,

GW, ML, MR, NE, SN, TD, TG

US 2004147531	A1	20040729	US 2003-731463		20031205
PRIORITY APPLN. INFO.:			US 2002-387001P	P	20020607
			US 2001-316761P	P	20010831
			US 2002-234643	A1	20020903

IT **500714-99-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of amidine derivs. for treating amyloidosis and neurodegenerative diseases)
RN 500714-99-8 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)-2-methylphenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



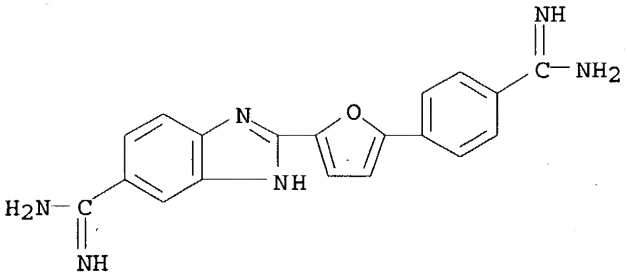
AB The present invention relates to the use of amidine compds. in the treatment of amyloid related diseases. In particular, the invention relates to a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound Among the compds. for use according to the invention are those according to the following Formulas, such that, when administered, amyloid fibril formation, neurodegeneration, or cellular toxicity is reduced or inhibited.

L4 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:851561 CAPLUS
DOCUMENT NUMBER:	139:392613
TITLE:	Cooperative Dimerization of a Heterocyclic Diamidine Determines Sequence-Specific DNA Recognition
AUTHOR(S):	Tanious, Farial; Wilson, W. David; Wang, Lei; Kumar, Arvind; Boykin, David W.; Marty, Carine; Baldeyrou, Brigitte; Bailly, Christian
CORPORATE SOURCE:	Department of Chemistry and Laboratory for Chemical and Biological Sciences, Georgia State University, Atlanta, GA, 30303, USA
SOURCE:	Biochemistry (2003), 42(46), 13576-13586 CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

IT **214216-29-2**, DB 293
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)
(cooperative dimerization of heterocyclic diamidine DB293 reflects sequence-specific DNA recognition by DB293)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-

furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



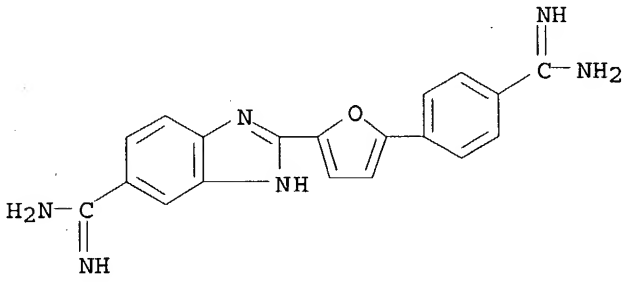
●2 HCl

AB In the course of a program aimed at discovering novel DNA-targeted antiparasitic drugs, the phenylfuran-benzimidazole unfused aromatic dication DB293 was identified as the first diamidine capable of forming stacked dimers in the DNA minor groove of GC-containing sequences. Its preferred binding sequence encompasses the tetranucleotide 5'-ATGA·5'-TCAT to which DB293 binds tightly with a strong pos. cooperativity. Here we have investigated the influence of the DNA sequence on drug binding using two complementary tech. approaches: surface plasmon resonance and DNase I footprinting. The central dinucleotide of the primary ATGA motif was systematically varied to represent all of the eight possible combinations (AXGA and ATYA, where X or Y = A, T, G, or C). Binding affinities for each site were precisely measured by SPR, and the extent of cooperative drug binding was also determined The sequence recognition process was found to be extremely dependent on the nature of the central dinucleotide pair. Modification of the central TG step decreases binding affinity by a factor varying from 2 to over 500 depending on the base substitution. However, the diminished binding affinity does not affect the unique binding mode. In nearly all cases, the SPR titrns. revealed a pos. cooperativity in complex formation which reflects the ease of the dication to form stacked dimeric motifs in the DNA minor groove. DNase I footprinting served to identify addnl. binding sites for DB293 in the context of long DNA sequences offering a large variety of randomly distributed or specifically designed sites. The ATGA motif provided the best receptor for the drug, but lower affinity sequences were also identified. The design of two DNA fragments composed of various targeted tetranucleotide binding sites separated by an "insulator" (nonbinding) sequence allowed us to delineate further the influence of DNA sequence on drug binding and to identify a novel high-affinity site: 5'-ACAA·5'-TTGT. Collectively, the SPR and footprinting results show that the consensus sequence 5'-(A/T)-TG-(A/T) represents the optimal site for cooperative dimerization of the heterocyclic diamidine DB293.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:831313 CAPLUS
DOCUMENT NUMBER: 141:225389
TITLE: Synthesis of analogs of 5-[2-(5-amidinobenzimidazoyl)]-2-(4-amidinophenyl)furan hydrochloride to test a DNA minor groove dimer binding model
AUTHOR(S): Batista-Parra, Adalgisa

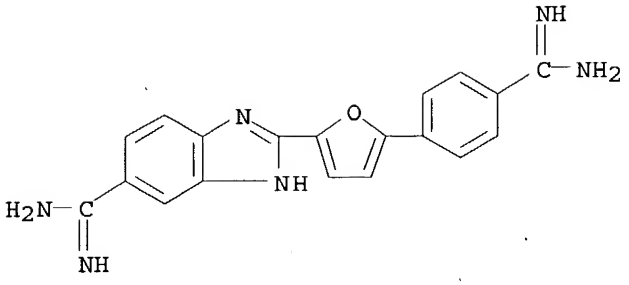
CORPORATE SOURCE: Georgia State Univ., Experiment, GA, USA
SOURCE: (2002) 87 pp. Avail.: UMI, Order No. DA3075417
From: Diss. Abstr. Int., B 2003, 63(12), 5843
DOCUMENT TYPE: Dissertation
LANGUAGE: English
IT **214216-29-2DP**, derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and DNA binding of)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



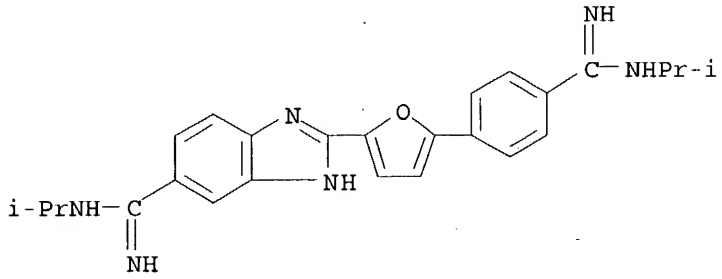
●2 HCl

AB Unavailable

L4 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:513253 CAPLUS
DOCUMENT NUMBER: 139:390750
TITLE: Detection of inhibition of bovine viral diarrhea virus by aromatic cationic molecules
AUTHOR(S): Givens, M. Daniel; Dykstra, Christine C.; Brock, Kenny V.; Stringfellow, David A.; Kumar, Arvind; Stephens, Chad E.; Goker, Hakan; Boykin, David W.
CORPORATE SOURCE: Department of Pathobiology, College of Veterinary Medicine, Auburn University, Auburn, AL, 36849, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2003), 47(7), 2223-2230
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:390750
IT **216308-19-9 216308-21-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of bovine viral diarrhea virus by aromatic cationic mols.)
RN 216308-19-9 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 216308-21-3 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[imino[(1-methylethyl)amino]methyl]phenyl]-2-furanyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



AB Bovine viral diarrhea virus (BVDV) is an economically significant pathogen of cattle and a problematic contaminant in the laboratory BVDV is often used as an in vitro model for hepatitis C virus during drug discovery efforts. Aromatic dicationic mols. have exhibited inhibitory activity against several RNA viruses. Thus, the purpose of this research was to develop and apply a method for screening the aromatic cationic compds. for in vitro cytotoxicity and activity against a noncytopathic strain of BVDV. The screening method evaluated the concentration of BVDV in medium and cell lysates after 72 h of cell culture in the presence of either a 25 or 5 μM concentration of the test compound Five of 93 screened compds. were selected for further determination of inhibitory (90 and 50%) and cytotoxic (50 and 10%) concentration endpoints. The screening method identified compds. that exhibited inhibition of BVDV at nanomolar concns. while exhibiting no cytotoxicity at 25 μM concns. The leading compds. require further investigation to determine their mechanism of action, in vivo activity, and specific activity against hepatitis C virus.

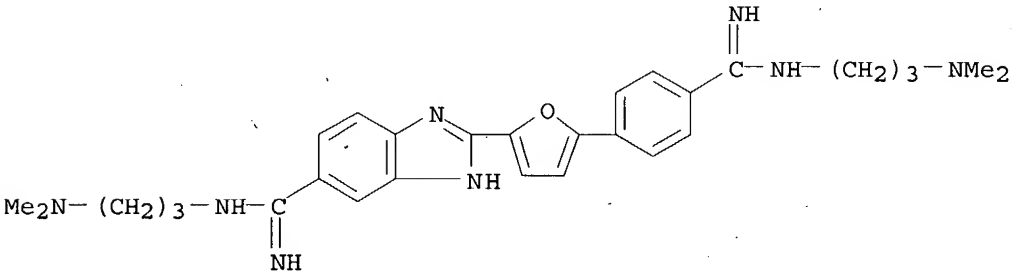
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:250479 CAPLUS
DOCUMENT NUMBER: 140:38649
TITLE: Application of molecular topology to the prediction of antifungal activity for a set of dication-substituted carbazoles, furans and benzimidazoles
AUTHOR(S): Garcia-Domenech, R.; Rios-Santamarina, I.; Catala, A.;

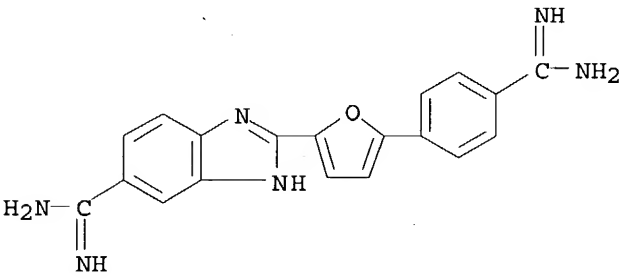
Calabuig, C.; del Castillo, L.; Galvez, J.
CORPORATE SOURCE: Facultat de Farmacia, Unidad de Investigacion de Conectividad Molecular y Diseno de Farmacos, Departamento de Quimica Fisica, Universitat de Valencia, Valencia, Spain
SOURCE: THEOCHEM (2003), 624, 97-107
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **213972-23-7 216308-19-9 216308-21-3 216308-25-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (mol. topol. in relation to antifungal activity for a set of dication-substituted carbazoles, furans, and benzimidazoles)

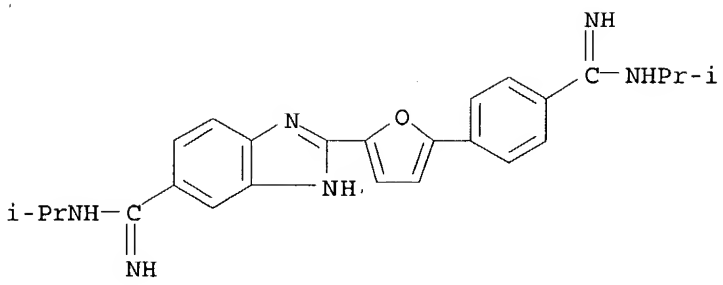
RN 213972-23-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



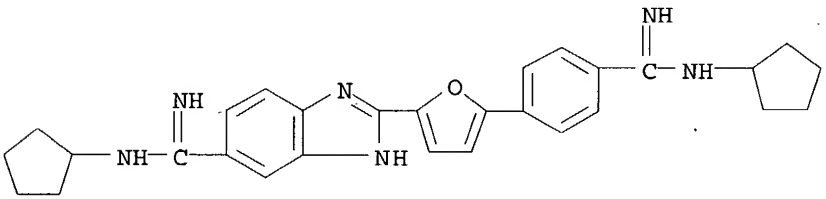
RN 216308-19-9 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



RN 216308-21-3 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[imino[(1-methylethyl)amino]methyl]phenyl]-2-furanyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 216308-25-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-cyclopentyl-2-[5-[4-[(cyclopentylamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



AB In this paper, the endpoint is the application of mol. topol. to the search of QSAR relations into a group of dication-substituted carbazoles, furans and benzimidazoles, all showing antifungal activity against C. albicans. Math. and statistical methods such as linear regression and discriminant anal., are used. The results clearly show a high efficiency of the formalism on the prediction and classification of antifungal activity. Some 83% of the compds. showing MIC <10 μg/mL (active group) are correctly classified, while 100% overall accuracy is achieved for those compds. showing MIC >100 μg/mL (inactive group).
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173414 CAPLUS
DOCUMENT NUMBER: 138:215350
TITLE: Amidine derivatives for treating amyloid-related diseases
INVENTOR(S): Chalifour, Robert J.; Kong, Xianqi; Wu, Xinfu; Lu, Wenshuo
PATENT ASSIGNEE(S): Neurochem Inc., Can.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017994	A1	20030306	WO 2002-CA1353	20020903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004006092	A1	20040108	US 2002-234643	20020903
EP 1420773	A1	20040526	EP 2002-758012	20020903

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2004147531	A1	20040729	US 2003-731463	20031205

PRIORITY APPLN. INFO.:

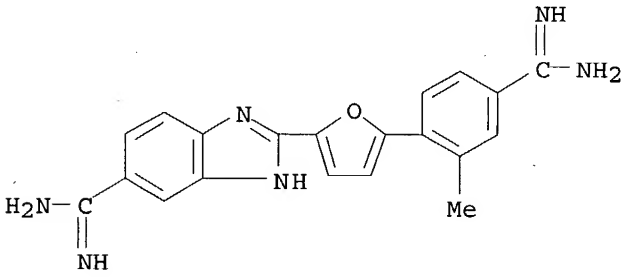
US 2001-316761P	P	20010831
US 2002-387001P	P	20020607
US 2002-234643	A1	20020903
WO 2002-CA1353	W	20020903

OTHER SOURCE(S): MARPAT 138:215350

IT **500714-99-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amidine derivs. for treating amyloid-related diseases)

RN 500714-99-8 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)-2-methylphenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



AB The invention discloses the use of amidine compds. in the treatment of amyloid-related diseases (e.g. Alzheimer's disease, Down's syndrome, type II diabetes). In particular, the invention discloses a method for treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound The compds. of the invention (Markush included) are such that, when administered, reduce or inhibit amyloid fibril formation, neurodegeneration, or cellular toxicity. Compound preparation is described.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:252822 CAPLUS

DOCUMENT NUMBER: 137:197

TITLE: Distribution of Furamidine Analogues in Tumor Cells: Influence of the Number of Positive Charges

AUTHOR(S): Lansiaux, Amelie; Dassonneville, Laurent; Facompre, Michaeel; Kumar, Arvind; Stephens, Chad E.; Bajic, Miroslav; Tanious, Farial; Wilson, W. David; Boykin, David W.; Bailly, Christian

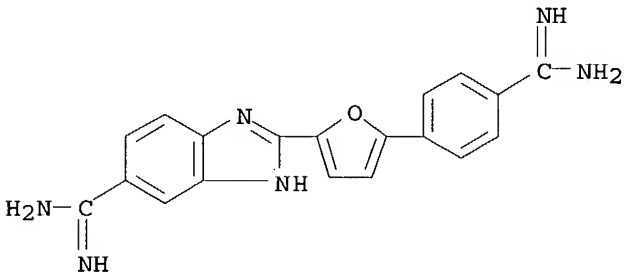
CORPORATE SOURCE: INSERM U-524 et Laboratoire de Pharmacologie

Antitumorale du Centre Oscar Lambret, IRCL, Lille, 59045, Fr.
SOURCE: Journal of Medicinal Chemistry (2002), 45(10), 1994-2002
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:197

IT **214216-29-2**, DB 293
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DB 293; synthesis and structure activity relationship of furamidine analogs in tumor cells and influence of number of pos. charges)

RN 214216-29-2 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

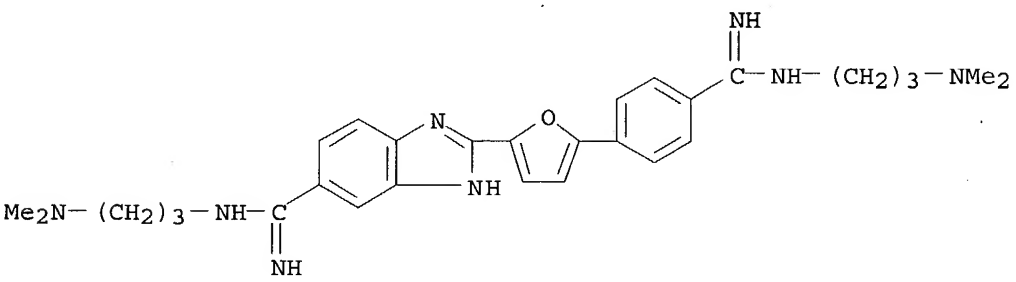


●2 HCl

IT **213972-23-7**, DB340
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and structure activity relationship of furamidine analogs in tumor cells and influence of number of pos. charges)

RN 213972-23-7 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

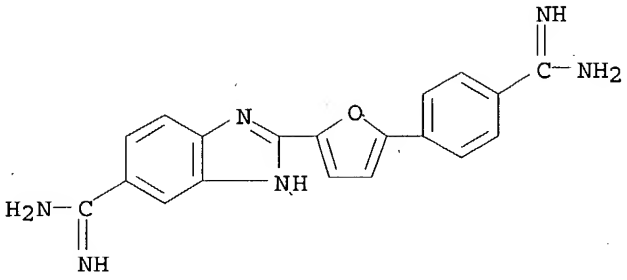


AB Fluorescence microscopy has been used to study the cellular distribution properties of a series of DNA binding cationic compds. related to the

potent antiparasitic drug furamidine (DB75). The compds. tested bear a diphenylfuran or a phenylfuranbenzimidazole unfused aromatic core substituted with one or two amidine or imidazoline groups. The synthesis of five new compds. is reported. The B16 melanoma cell line was used to compare the capacities of mono-, bis-, and tetracations to enter the cell and nuclei. The high-resolution fluorescence pictures show that in the furamidine series, the compds. with two or four pos. charges selectively accumulate in the cell nuclei whereas, in most cases, those bearing only one pos. charge show reduced cell uptake capacities. One of the monocationic compds., DB607, distributes in the cytoplasm, possibly in mitochondria, with no distinct nuclear accumulation. In sharp contrast, furamidine and benzimidazole analogs, including the drug DB293 that forms DNA minor groove dimers, efficiently accumulate in the cell nuclei and the intranuclear distribution of these DNA minor groove binders is significantly different from that seen with the DNA intercalating drug propidium iodide. The results suggest that the presence of two amidine terminal groups plays a role in facilitating nuclear accumulation into cells, probably as a result of nucleic acid binding. The determination of DNA melting temperature increases on addition of these compds. supports the importance of DNA binding in nuclear uptake.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:235444 CAPLUS
DOCUMENT NUMBER: 137:59097
TITLE: Comparative Thermodynamics for Monomer and Dimer Sequence-dependent Binding of a Heterocyclic Dication in the DNA Minor Groove
AUTHOR(S): Wang, Lei; Kumar, Arvind; Boykin, David W.; Bailly, Christian; Wilson, W. David
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Journal of Molecular Biology (2002), 317(3), 361-374
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **214216-29-2**, DB 293
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(DB 293; comparative thermodn. for monomer and dimer sequence-dependent binding of a heterocyclic dication in the DNA minor groove)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

AB Phenylamidine cationic groups linked by a furan ring (furamidine) and related sym. diamidine compds. bind as monomers in the minor groove of AT sequences of DNA. DB293, an unsym. derivative with one of the Ph rings of furamidine replaced with a benzimidazole, can bind to AT sequences as a monomer but binds more strongly to GC-containing minor-groove DNA sites as a stacked dimer. The dimer-binding mode has high affinity, is highly cooperative and sequence selective. In order to develop a better understanding of the correlation between structural and thermodn. aspects of DNA mol. recognition, DB293 was used as a model to compare the binding of minor-groove agents with AT and mixed sequence DNA sites. Isothermal titration calorimetry and surface plasmon resonance results clearly show that the binding of DB293 and other related compds. into the minor groove of AT sequences is largely entropy-driven while the binding of DB293 as a dimer into the minor groove of GC-containing sequences is largely enthalpy-driven. At 25°, for example, the AT binding has ΔG°, ΔH° and TΔS° values of -9.6, -3.6 and 6.0 kcal/mol while the values for dimer binding to a GC-containing site are -9.0, -10.9 and -1.9 kcal/mol (per mol. of bound compound), resp. These results show that the thermodn. components for binding of compds. of this type to DNA are very dependent on the structure, solvation and sequence of the DNA binding site.

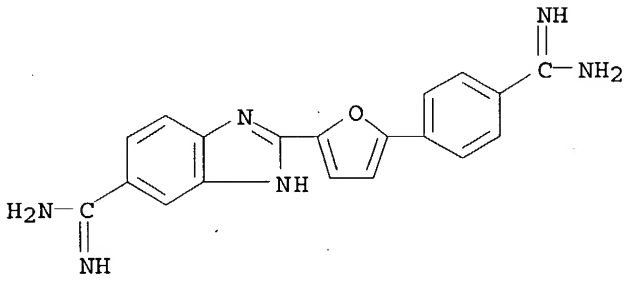
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:651648 CAPLUS
DOCUMENT NUMBER: 136:211412
TITLE: The hybridization-stabilization assay: a solution-based isothermal method for rapid screening and determination of sequence preference of ligands that bind to duplexed nucleic acids
AUTHOR(S): Gonzalez, Carolyn; Moore, Megan; Ribeiro, Sofia; Schmitz, Uli; Schroth, Gary P.; Turin, Lisa; Bruice, Thomas W.
CORPORATE SOURCE: Genelabs Technologies Inc., Redwood City, CA, 94063, USA
SOURCE: Nucleic Acids Research (2001), 29(16), e85/1-e85/13
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **214216-29-2**, DB 293
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);

ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hybridization-stabilization assay, a solution-based isothermal method for rapid screening and determination of sequence preference of ligands that bind
to duplexed nucleic acids)

RN 214216-29-2 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

AB The gene-to-drug quest will be most directly served by the discovery and development of small mols. that bind to nucleic acids and modulate gene expression at the level of transcription and/or inhibit replication of infectious agents. Full realization of this potential will require implementation of a complete suite of modern drug discovery technologies. Towards this end, here we describe our initial results with a new assay for identification and characterization of novel nucleic acid binding ligands. It is based on the well recognized property of stabilization of hybridization of complementary oligonucleotides by groove and/or intercalation binding ligands. Unlike traditional thermal melt methodologies, this assay is isothermal and, unlike gel-based footprinting techniques, the assay also is performed in solution and detection can be by any number of highly sensitive, non-radioisotopic modalities, such as fluorescence resonance energy transfer, described herein. Thus, the assay is simple to perform, versatile in design and amenable to miniaturization and high throughput automation. Assay validation was performed using various permutations of direct and competitive binding formats and previously well studied ligands, including pyrrole polyamide and intercalator natural products, designed hairpin pyrrole-imidazole polyamides and furan-based non-polyamide dications. DNA specific ligands were identified and their DNA binding site size and sequence preference profiles were determined A systematic approach to studying the relationship of binding sequence specificity with variation in ligand structure was demonstrated, and preferred binding sites in longer DNA sequences were found by pseudo-footprinting, with results that are in accord with established findings. This assay methodol. should promote a more rapid discovery of novel nucleic acid ligands and potential drug candidates.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:534585 CAPLUS

DOCUMENT NUMBER: 135:118379

TITLE: Recognition of ATGA Sequences by the Unfused Aromatic

Dication DB293 Forming Stacked Dimers in the DNA Minor Groove

AUTHOR(S): Bailly, Christian; Tardy, Christelle; Wang, Lei; Armitage, Bruce; Hopkins, Katherine; Kumar, Arvind; Schuster, Gary B.; Boykin, David W.; Wilson, W. David

CORPORATE SOURCE: INSERM U-524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Lille, 59045, Fr.

SOURCE: Biochemistry (2001), 40(33), 9770-9779
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

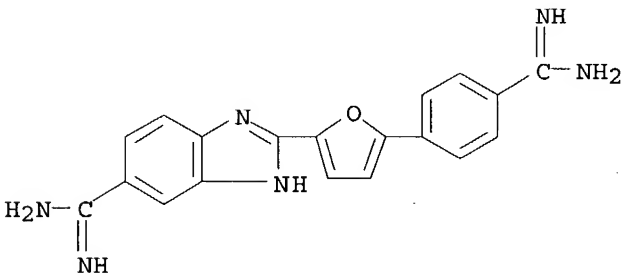
DOCUMENT TYPE: Journal

LANGUAGE: English

IT **214216-29-2**, DB 293
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(delineating the nature of DNA sequences recognized by phenylfuranbenzimidazole diamidine derivative DB293, and relationship between sequence of binding and stoichiometry of drug-DNA interaction)

RN 214216-29-2 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



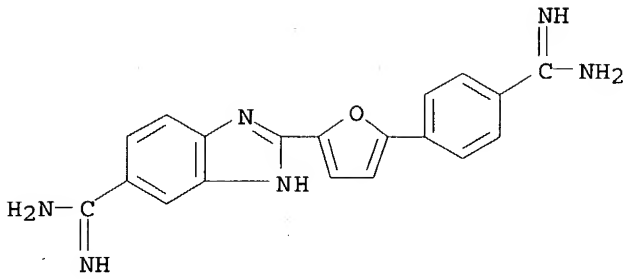
●2 HCl

AB Furamidine and related diamidines represent a promising series of drugs active against widespread parasites, in particular the Pneumocystic carinii pathogen. In this series, the phenylfuranbenzimidazole diamidine derivative DB293 was recently identified as the first unfused aromatic dication capable of forming stacked dimers in the DNA minor groove of GC-containing sequences. Here we present a detailed biochem. and biophys. characterization of the DNA sequence recognition properties of DB293. Three complementary footprinting techniques using DNase I, FeII-EDTA, and an anthraquinone photonuclease were employed to locate binding sites for DB293 in different DNA restriction fragments. Two categories of sites were identified by DNase I footprinting: (i) 4/5 bp sequences containing contiguous A·T pairs, such as 5'-AAAA and 5'-ATTA; and (ii) sequences including the motif 5'-ATGA·5'-TCAT. In particular, a 13-bp sequence including two contiguous ATGA motifs provided a highly preferential recognition site for DB293. Quant. footprinting anal. revealed better occupancy of the 5'-ATGA site compared to the AT-rich sites. Preferential binding of DB293 to ATGA sites was also observed with other DNA fragments and was confirmed independently by means of hydroxyl radical footprinting generated by the FeII-EDTA system, as well as by a photofootprinting approach using the probe anthraquinone-2-sulfonate

(AQS). In addition, this photosensitive reagent revealed the presence of sites of enhanced cutting specific to DB293. This mol., but not other minor groove binders such as netropsin, induces specific local structural changes in DNA near certain binding sites, as independently shown by DNase I and the AQS probe. Recognition of the ATGA sequence by DB293 was investigated further using melting temperature expts. and surface plasmon resonance (SPR). The use of different hairpin oligonucleotides showed that DB293 can interact with AT sites via the formation of 1:1 drug-DNA complexes but binds much more strongly, and cooperatively, to ATGA-containing sequences to form 2:1 drug-DNA complexes. DB293 binds strongly to ATGA sequences with no significant context dependence but is highly sensitive to the orientation of the target sequence. The formation of 2:1 DB293/DNA complexes is abolished by reversing the sequence 5'-ATGA→3'-ATGA, indicating that directionality plays an important role in the drug-DNA recognition process. Similarly, a single mutation in the A[T→G]GA sequence is very detrimental to the dimer interactions of DB293. From the complementary footprinting and SPR data, the 5'-ATGA sequence is identified as being a highly favored dimer binding site for DB293. The data provide clues for delineating a recognition code for diamidine-type minor groove binding agents, and ultimately to guide the rational design of gene regulatory mols. targeted to specific sites of the genetic material.

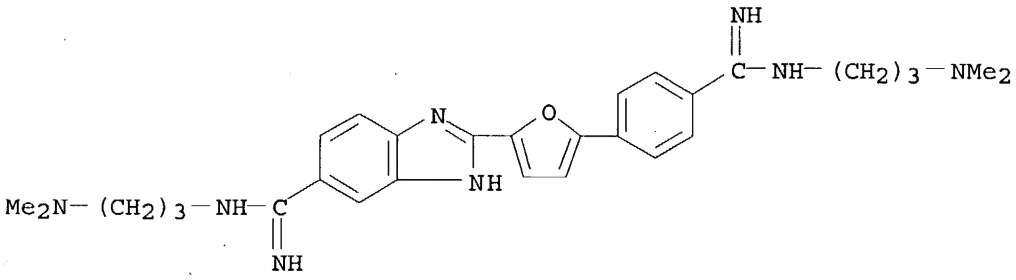
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:373395 CAPLUS
DOCUMENT NUMBER: 135:251448
TITLE: Inhibition of the HIV-1 Rev-RRE complex formation by unfused aromatic cations
AUTHOR(S): Xiao, G.; Kumar, A.; Li, K.; Rigl, C. T.; Bajic, M.; Davis, T. M.; Boykin, D. W.; Wilson, W. D.
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(5), 1097-1113
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **214216-29-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DB 293; preparation of and inhibition of the HIV-1 Rev-RRE complex formation by unfused aromatic cations)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

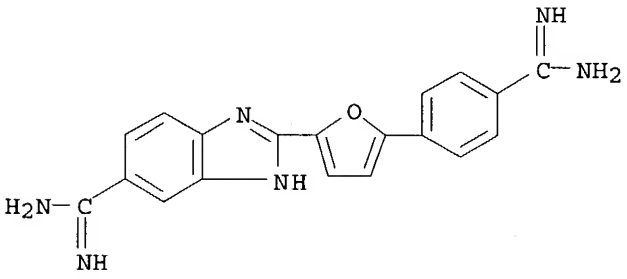
IT **213972-23-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DB 340; preparation of and inhibition of the HIV-1 Rev-RRE complex formation by unfused aromatic cations)
RN 213972-23-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



AB RNA viruses cause a wide range of human diseases. Development of new agents to target such viruses is an active area of research. Toward this goal, a series of diphenylfuran cations as potential inhibitors of the Rev-RRE complex have been designed and synthesized. Anal. of the interaction of the diphenylfurans with RRE and TAR RNA model systems by gel shift assays indicates that they exhibit both sequence and structure-dependent binding modes. Our results show a strong interaction between the diphenylfuran ring system and RRE bases, while the TAR interactions are much weaker with the compds. that are the best inhibitors of Rev-RRE. A diphenylfuran lead compound was systematically varied and the ability of the new compds. to inhibit the formation of Rev-RRE and Tat-TAR complexes was assayed by gel-mobility shift expts. In this series, DB340 was found to be the most active compound and also the most specific compound for inhibition of Rev-RRE complex formation.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

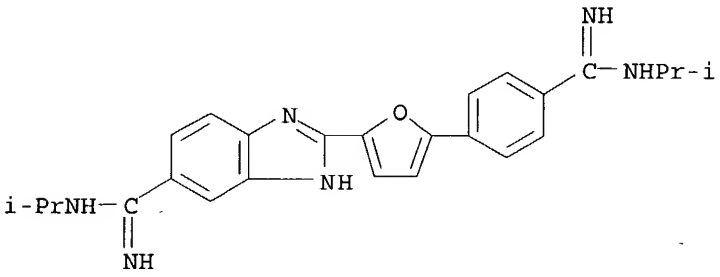
L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:79423 CAPLUS
DOCUMENT NUMBER: 134:277012
TITLE: Evaluation of the Influence of Compound Structure on Stacked-Dimer Formation in the DNA Minor Groove
AUTHOR(S): Wang, Lei; Carrasco, Carolina; Kumar, Arvind; Stephens, Chad E.; Bailly, Christian; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Biochemistry (2001), 40(8), 2511-2521
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:277012
IT **214216-29-2**, DB 293 **216308-21-3**, DB 294
216308-25-7, DB 331
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(preparation and evaluation of the influence of heterocyclic dication compound
structure on stacked-dimer formation in the DNA minor groove)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)

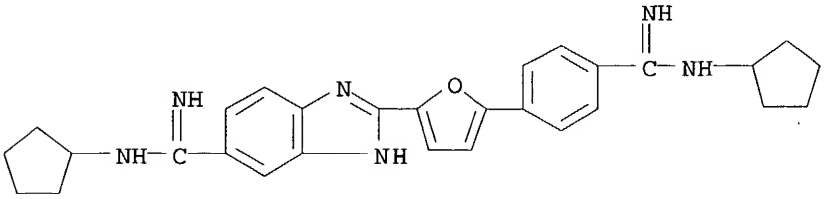


●2 HCl

RN 216308-21-3 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[imino[(1-methylethyl)amino]methyl]phenyl]-2-furanyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 216308-25-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-cyclopentyl-2-[5-[4-[(cyclopentylamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



AB The Human Genome Project as well as sequencing of the genomes of other organisms offers a wealth of DNA targets for both therapeutic and diagnostic applications, and it is important to develop addnl. DNA binding motifs to fully exploit the potential of this new information. We have recently found that an aromatic dication, DB293, with an amidine-phenyl-furan-benzimidazole-amidine structure can recognize specific sequences of DNA by binding in the minor groove as a dimer. The dimer binding is strong, highly cooperative and, in contrast to many closely related heterocyclic dications, has both GC and AT base pairs in the minor groove binding site. The aromatic heterocycle stacked dimer is quite different in structure from the polyamide-lexitropsin type compds., and it is a dication while all lexitropsin dimers are monocations. The heterocyclic dimer represents only the second small mol. class that can recognize mixed sequences of DNA. To test the structural limits on the new type of complex, it is important to probe the influence of compound charge, chemical groups, and structural features. The effects of these compound mol. variations on DNA complex formation with several DNA sequences were evaluated by DNase I footprinting, CD and UV spectroscopy, thermal melting, and quant. anal. with surface plasmon resonance biosensor methods. Conversion of the amidines to guanidinium groups does permit the cooperative dimer to form but removal of one amidine or addition of an alkyl group to the amidine strongly inhibited dimer formation. Changing the Ph of DB293 to a benzimidazole or the benzimidazole to a Ph or benzofuran also inhibited dimer formation. The results show that formation of the minor groove stacked-dimer complex is very sensitive to compound structure. The discovery of the aromatic dimer mode offers new opportunities to enhance the specificity and expand the range of applications of the compds. that target DNA.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

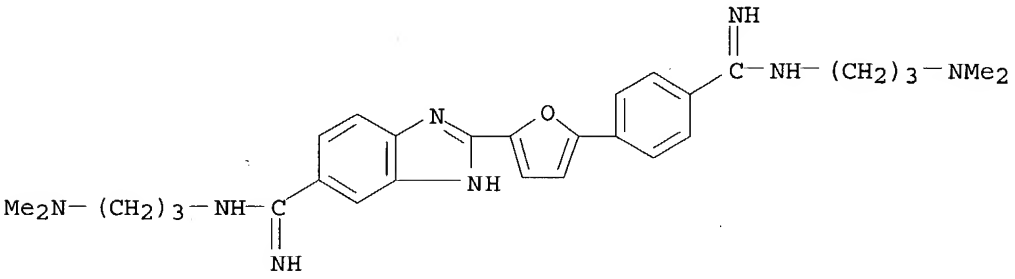
L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:28129 CAPLUS
DOCUMENT NUMBER: 134:217165
TITLE: A Heterocyclic Inhibitor of the Rev-RRE Complex Binds to RRE as a Dimer
AUTHOR(S): Li, Ke; Davis, Tina M.; Bailly, Christian; Kumar, Arvind; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: Department of Chemistry and Laboratory for Chemical and Biological Sciences, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Biochemistry (2001), 40(5), 1150-1158
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

IT **213972-23-7**, DB 340
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(heterocyclic inhibitor of rev-RRE complex binds to HIV-1 RRE as a dimer in relation to targeting RNA and drug design)

RN 213972-23-7 CAPLUS

CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



AB As part of a search for organic compds. that selectively target RNA, the authors found that specific diphenylfuran derivs., which are related to compds. that bind to the DNA minor groove, bind very strongly to RNA in a manner very sensitive to the structure of the compds. In extended development of the diphenylfuran series, the authors found that a tetracationic heterocycle containing a phenyl-furan-benzimidazole unfused aromatic system, DB340, exhibits pronounced selectivity for the RRE RNA stem-loop from HIV-1. The authors report here RNA footprinting, spectroscopic anal., affinity detns., and initial NMR structural results of the complex. The results indicate that DB340 binds to RRE in a highly structured and cooperative complex at a 2:1 DB340 to RRE ratio. Overlap in the NMR spectra prevents detailed description of binding interactions at this time, but the authors are able to place DB340 in the RNA minor groove. Addnl., footprinting results and studies with mutant RRE sequences indicate that the internal loop of RRE is required for specific binding of DB340 as with the Rev protein. These results provide exciting new ideas for rational drug design with RNA as is now common with DNA and proteins.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:359151 CAPLUS

DOCUMENT NUMBER: 133:159909

TITLE: A novel solid-phase assembly for identifying potent and selective RNA ligands

AUTHOR(S): Luedtke, Nathan W.; Tor, Yitzhak

CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0358, USA

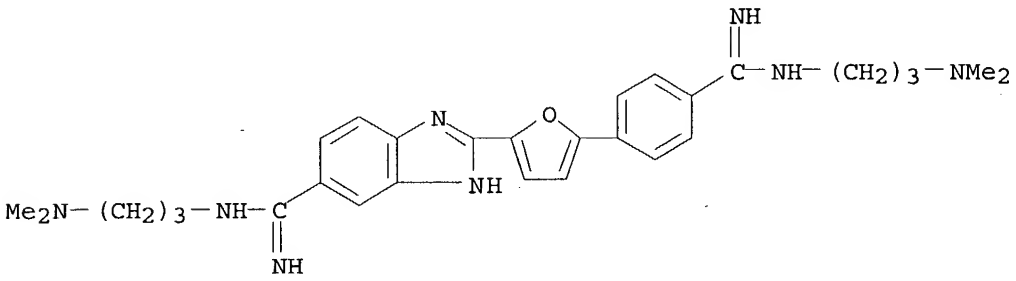
SOURCE: Angewandte Chemie, International Edition (2000), 39(10), 1788-1790
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

IT **213972-23-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(a novel solid-phase assembly for identifying potent and selective RNA ligands)
RN 213972-23-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

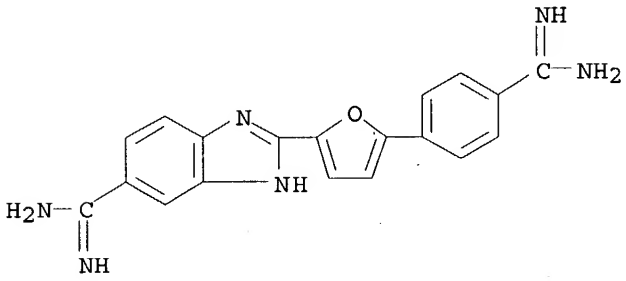


AB Replication of the human immunodeficiency virus (HIV-1) requires an ordered pattern of viral gene expression. This process is dependent upon the association of Rev, an essential viral regulatory protein, with its resp. RNA binding site, the Rev-response-element (RRE). Small mols. that specifically bind the RRE and preclude or competitively displace the Rev protein are therefore promising antiviral candidates. New approaches that allow the rapid determination of both the RNA affinity and specificity of small mols. will assist in the discovery of new lead compds. and advance the understanding of RNA recognition. To this end, we report the assembly of an immobilized RNA-protein complex and demonstrate its application to the discovery and characterization of new RNA binders. We have developed an assay that identifies small mols. that specifically interfere with Rev-RRE binding. To examine the versatility of the assembly-based assay the competitive binding of polycyclic aromatic amidines to the RRE has also been examined This family of ligands is more potent than aminoglycosides. Their previously reported trend in RRE affinity is again accurately reproduced. A tenfold increase in IC50 values in the presence of competing DNA indicates that these compds. also have a relatively high affinity for double-stranded DNA. This result clearly illustrates how the observed potency of an inhibitor is influenced by its selectivity. Both selectivity and affinity are crucial for the design and evaluation of new RNA-protein inhibitors.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:38461 CAPLUS
DOCUMENT NUMBER: 132:218461
TITLE: Specific molecular recognition of mixed nucleic acid sequences: an aromatic dication that binds in the DNA minor groove as a dimer
AUTHOR(S): Wang, Lei; Bailly, Christian; Kumar, Arvind; Ding, Daoyuan; Bajic, Miroslav; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (2000), 97(1), 12-16
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **214216-29-2**, DB 293
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(DNA recognizing organic cation; aromatic dications that bind sequence-specifically to DNA minor groove)
RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

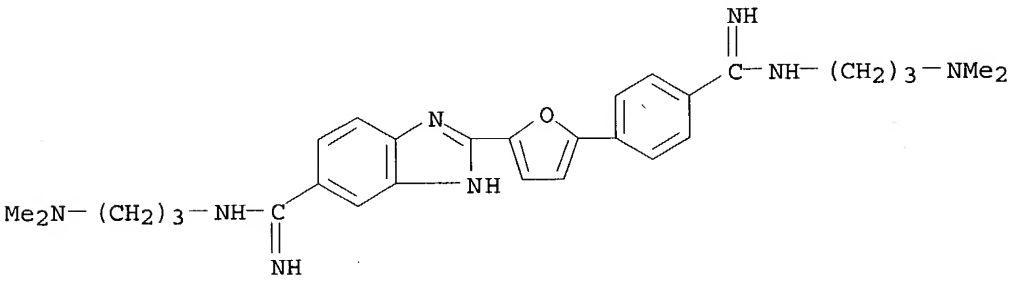
AB Phenylamidine cationic groups linked by a furan ring (furamidine) and related compds. bind as monomers to AT sequences of DNA. An unsym. derivative (DB293) with one of the Ph rings of furamidine replaced with a benzimidazole has been found by quant. footprinting analyses to bind to GC-containing sites on DNA more strongly than to pure AT sequences. NMR structural anal. and surface plasmon resonance binding results clearly demonstrate that DB293 binds in the minor groove at specific GC-containing sequences of DNA in a highly cooperative manner as a stacked dimer. Neither the sym. bisphenyl nor bisbenzimidazole analogs of DB293 bind significantly to the GC containing sequences. DB293 provides a paradigm for design of compds. for specific recognition of mixed DNA sequences and extends the boundaries for small mol.-DNA recognition.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:664986 CAPLUS
DOCUMENT NUMBER: 130:22621
TITLE: In vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles
AUTHOR(S): Del Poeta, Maurizio; Schell, Wiley A.; Dykstra, Christine C.; Jones, Susan K.; Tidwell, Richard R.; Kumar, Arvind; Boykin, David W.; Perfect, John R.
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2503-2510

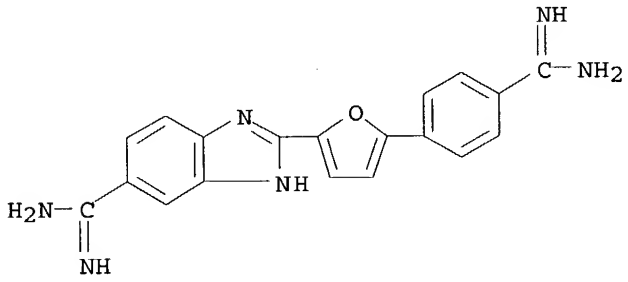
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **213972-23-7 216308-19-9 216308-21-3 216308-25-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antifungal activities of a series of dication-substituted carbazoles, furans, and benzimidazoles)

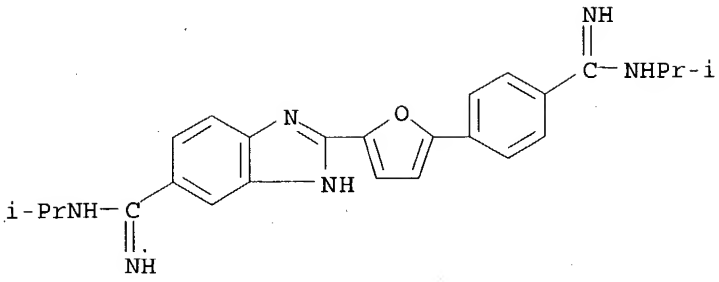
RN 213972-23-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



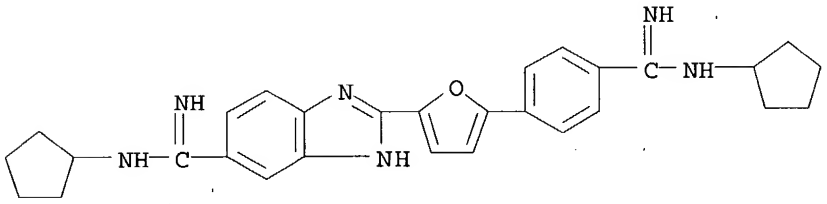
RN 216308-19-9 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



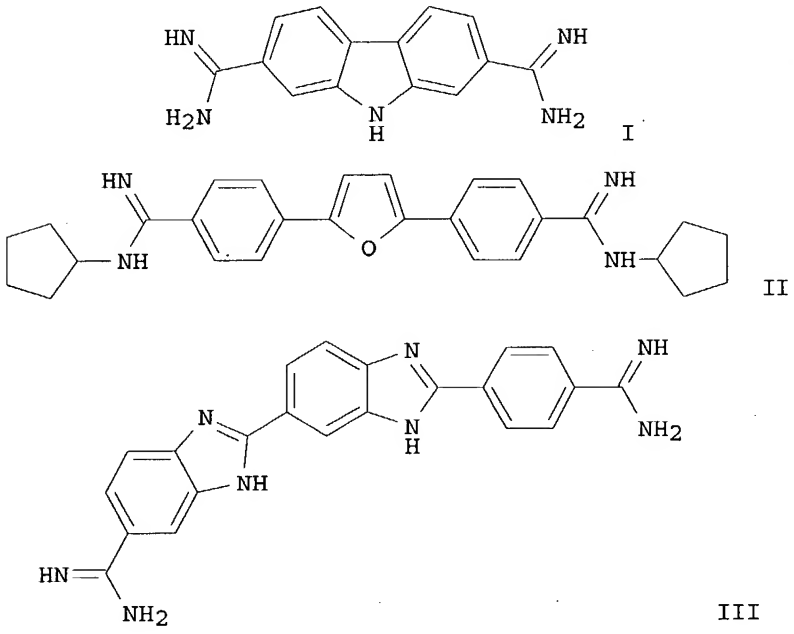
RN 216308-21-3 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[imino[(1-methylethyl)amino]methyl]phenyl]-2-furanyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)



RN 216308-25-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-cyclopentyl-2-[5-[4-[(cyclopentylamino)iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)



GI



I

II

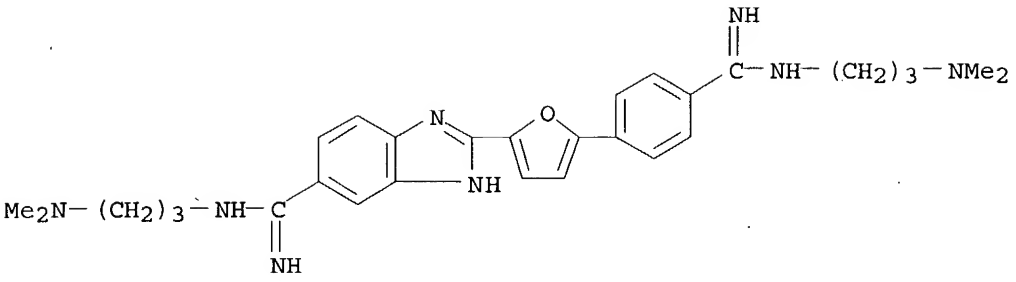
III

AB Aromatic dicationic compds. possess antimicrobial activity against a wide range of eucaryotic pathogens, and in the present study an examination of the

structures-functions of a series of compds. against fungi was performed. Sixty-seven dicationic mols. were screened for their inhibitory and fungicidal activities against Candida albicans and Cryptococcus neoformans. The MICs of a large number of compds. were comparable to those of the standard antifungal drugs amphotericin B and fluconazole. Unlike fluconazole, potent inhibitory compds. in this series were found to have excellent fungicidal activities. Broad-spectrum activities were observed for the carbazole I, the furan II, and the benzimidazole III. The MIC of III, one of the most potent compds., against C. albicans was 0.39 μg/mL, and it was the most potent compound against C. neoformans (MIC, ≤0.09 μg/mL). Selected compds. were also found to be active against Aspergillus fumigatus, Fusarium solani, Candida species other than C. albicans, and fluconazole-resistant strains of C. albicans and C. neoformans. Since of these compds. have been safely given to animals, these classes of mols. have the potential to be developed as antifungal agents.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:606581 CAPLUS
DOCUMENT NUMBER: 129:285585
TITLE: Design and analysis of organic cations that inhibit interactions of the HIV-1 Rev protein with RRE RNA
AUTHOR(S): Li, Ke; Xiao, Ge; Rigl, Ted; Kumar, Arvind; Boykin, David W.; Wilson, W. David
CORPORATE SOURCE: Department of Chemistry, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Structure, Motion, Interaction and Expression of Biological Macromolecules, Proceedings of the Conversation in the Discipline Biomolecular Stereodynamics, 10th, Albany, June 17-21, 1997 (1998), Meeting Date 1997, Volume 2, 137-145. Editor(s): Sarma, Ramaswamy H.; Sarma, Mukti H. Adenine Press: Schenectady, N. Y.
CODEN: 66NGAV
DOCUMENT TYPE: Conference
LANGUAGE: English
IT **213972-23-7**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(design and anal. of organic cations that inhibit interactions of the HIV-1 Rev protein with RRE RNA)
RN 213972-23-7 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-[3-(dimethylamino)propyl]-2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]- (9CI) (CA INDEX NAME)

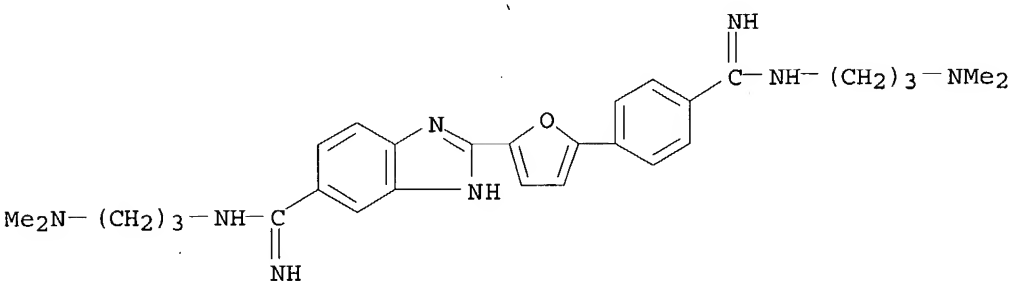


AB Specific interactions of regulatory proteins, such as HIV-1 Rev and Tat, with RNA, such RRE and TAR, are essential for viral replication. Small mols. that bind specifically to RRE or TAR RNA and interfere with the protein-RNA interactions are thus potential antiviral agents. We have found that certain tetracationic diphenylfuran derivs. bind to the RRE RNA and inhibit Rev-RRE interaction. In order to define the structural features that are essential for RNA binding and to improve the inhibitory activity, we have designed addnl. diphenylfuran analogs with structural changes at the cationic substituents as well as the central aromatic rings, and have analyzed the RRE binding activity and the inhibition of Rev-RRE interaction by these new compds. Our results show that the cationic groups in diphenylfuran tetracationic compds. are essential for RNA binding. Replacing the amidines with amide groups or removing the terminal amino groups results in loss of activity. On the other hand, structural modifications of the unfused furan and Ph rings lead to compds. with significantly increased activity. The best compound, in which one of the Ph rings of the diphenylfuran moiety is replaced by a benzimidazole function, binds very strongly to the model RRE hairpin with a KD of 1.8 nM and exhibited potent inhibition of Rev-RRE complex formation in a gel shift assay. Structure-activity relationship anal. provides information on binding interactions of these organic cations with the RNA target which should be helpful to the design of more potent inhibitor. Our results further demonstrate the feasibility of highly potent and specific inhibition of protein-RNA interactions by small mols.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:589854 CAPLUS
DOCUMENT NUMBER: 129:299454
TITLE: Strategies for inhibition of RNA-protein complexes: from small molecules to nucleic acid decoys
AUTHOR(S): Wilson, W. David; Xiao, Ge; Li, Ke; Kumar, Arvind; Boykin, David W.; Ding, Daoyuan; Rigl, Ted; Manoharan, Muthiah; Gryaznov, Sergei
CORPORATE SOURCE: Chemistry Department, Georgia State University, Atlanta, GA, 30303, USA
SOURCE: Nucleic Acids Symposium Series (1998), 39, 135-136
CODEN: NACSD8; ISSN: 0261-3166
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **214598-02-4**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(strategies for development of virucides that inhibit viral RNA-protein

complexes)
RN 214598-02-4 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[[[3-(dimethylamino)propyl]amino]iminomethyl]phenyl]-2-furanyl]-N-[3-(dimethylamino)propyl]-, conjugate tetraacid (9CI) (CA INDEX NAME)

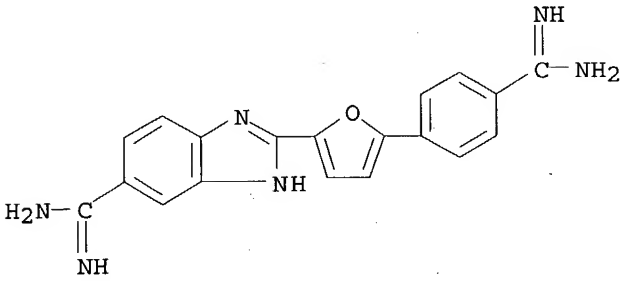


● 4 H^+

AB RNA viruses cause a wide range of human diseases and development of new agents to target such viruses is an active area of research. We are pursuing the development of organic cations that target the RNA of important viral RNA protein complexes as well as modified nucleic acids that target the protein component of the complex. We have designed un-fused aromatic cations that bind strongly and selectively to the RRE RNA of HIV-1 and inhibit its complex with Rev. A-form nucleic acids that are nuclease stable and mimic the folded structure of RRE have also been found to strongly bind Rev and inhibit the RRE-Rev complex.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

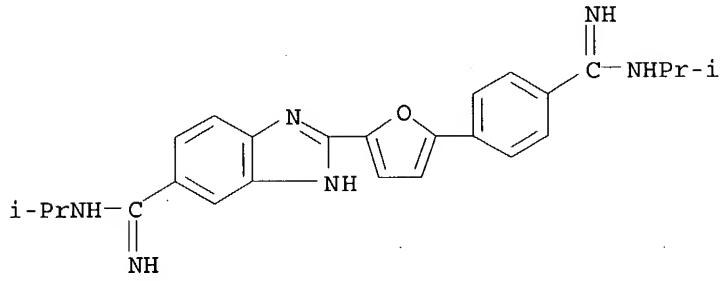
L4 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:586991 CAPLUS
DOCUMENT NUMBER: 129:290089
TITLE: Extended Aromatic Furan Amidino Derivatives as Anti-Pneumocystis carinii Agents
AUTHOR(S): Hopkins, Katherine T.; Wilson, W. David; Bender, Brendan C.; McCurdy, Donald R.; Hall, James Edwin; Tidwell, Richard R.; Kumar, Arvind; Bajic, Miro; Boykin, David W.
CORPORATE SOURCE: Department of Chemistry and Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA, 30303-3083, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(20), 3872-3878
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:290089
IT **214216-29-2P 214216-30-5P 214216-31-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of bis[(alkylamidino)phenyl]furans for treatment of Pneumocystis carinii infections)

RN 214216-29-2 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-(aminoiminomethyl)phenyl]-2-furanyl]-, dihydrochloride (9CI) (CA INDEX NAME)



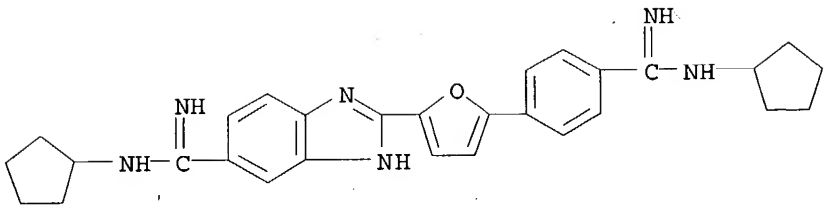
●2 HCl

RN 214216-30-5 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, 2-[5-[4-[imino[(1-methylethyl)amino]methyl]phenyl]-2-furanyl]-N-(1-methylethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 214216-31-6 CAPLUS
CN 1H-Benzimidazole-5-carboximidamide, N-cyclopentyl-2-[5-[4-[(cyclopentylamino)iminomethyl]phenyl]-2-furanyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

AB The syntheses of nine new derivs. of 2,5-bis[4-(N-alkylamidino)phenyl]furans with extended aromatic systems are reported. The interaction of these dicationic furans with poly(dA)*poly(dT) and with the duplex oligomers d(CGCGAATTCGCG)2 and d(GCGAATTCGC)2 was determined by Tm measurement, and the effectiveness of these compds. against the immunosuppressed rat model of Pneumocystis carinii was evaluated. At a screening dose of 10 μmol/kg, 4 of the 12 amidino furans described here are more active than the parent 2,5-Bis(4-aminidophenyl)furan. In general, extension of the aromatic system in the absence of a substitution of the amidino nitrogens resulted in higher affinity for DNA than the parent compound as judged by the larger ΔTm values and suggests enhanced van der Waals interactions in the amidino furan-DNA complex. One of the compds., 2,5-Bis[[4-(cyclopentyl)amidino]phenyl]furan (I) yielded cysts counts of less than 0.1% of control when administered at a dosage of 10 μmol/kg. I, which does not have an extended aromatic system, is the most active derivative Although a direct correlation between anti-P. carinii activity and DNA binding affinity was not observed, all compds. which have significant activity have large ΔTm values.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	94.15	250.20

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-13.30	-13.30

STN INTERNATIONAL LOGOFF AT 14:28:41 ON 05 NOV 2004